Amino acids – derived from dietary protein – absorbed from intestine through blood – taken up by tissues – used for

- biosynthesis of body protein
- oxidized to yield energy

Body protein always undergo turnover – constantly being synthesized and degraded

The AA released by body protein breakdown – enter the same pool of AA as the AA from the diet

AA also used for synthesis of N-containing compound
Metabolism of amino acid - more complex compared to carbohydrate and lipid metabolism

In normal diet, 60-100 g proteins- most are used for synthesis of proteins in liver and other tissues

Excessive amino acids in the diet – converted to glucose (energy) → fatty acid → t a g (energy depot)
Amino acid required for

- Biosynthesis of proteins
- precursor for N compounds
- oxidized - N atom → urea
  - C atom → - CH (glucose)
    - acetyl CoA – ketone bodies, fatty acid
  - non essential amino acid
Amino acids – 20 AA forming protein in nature

- Essential AA – must be present in the diet – can not be synthesized

- Non essential AA – can be formed by transamination of metabolic intermediates
11 from 20 AA-forming protein – can be synthesized in our body (non essential AA)

- 10 AA $\rightarrow$ can be synthesized from glucose
  - ser $\rightarrow$ asn
  - gly $\rightarrow$ glu
  - cys $\rightarrow$ gln
  - ala $\rightarrow$ pro
  - asp $\rightarrow$ arg

- 1 AA $\rightarrow$ synthesized from essential AA
  - phe $\rightarrow$ tyr
- 9 AA → essential → must be present in our diet → its C atom – can not be synthesized
- lys - trp
- ile - phe
- leu - met
- thr - his
- val - *arg
(L I L  T V  T O  P M  H A)

• Arg → semi essential
  - children → essential
  - adult → synthesis from urea cycle
DEGRADATION of AMINO ACIDS

- their carbons converted to
  - CO₂
  - compounds that produce glucose in the liver
    (pyruvate, α-KG, succ CoA, fumarate, oxaloacetate)
  - ketone bodies

- glucogenic a.a - if their C converted to glc
- ketogenic a.a - if their C converted to acetyl CoA or acetoacetate
METABOLISM OF CARBON ATOM AA

11 non essential AA

- 10 AA – can be formed from glucose – through intermediate of glycolysis and TCA
  - 4 AA – from glycolysis intermediate
    - ser – cys
    - gly – ala
  - 6 AA – from TCA cycle intermediate
    - glu, gln, pro, arg – from α-KG
    - asp, asn – from oxaloacetate
In fasting

-most of AA → pyruvate, intermediate of TCA cycle, acetyl CoA → formed glucose or ketone bodies → blood → energy for the tissues → CO\(_2\) + H\(_2\)O + ATP
AA synthesized from intermediate of glycolysis (non essential A) - produced pyruvate on degradation

A synthesized from intermediate of Krebs cycle - produced this intermediate during degradation
Glucogenic amino acids

- **tryptophane** → produced alanine → converted to pyruvate → glucose

- **methionine, threonine, valine, isoleucine** → succynil CoA → glucose

- **Phenyl alanine** → converted to tyrosine → fumarate → glucose
Glucogenic and ketogenic amino acids:
- tryptophane, isoleucine, threonine $\rightarrow$ acetyl CoA
- phenyl alanine $\rightarrow$ acetoacetate

Ketogenic amino acids:
- lysine, leucine
**During fasting** – muscle proteins were degraded to amino acids – some were oxidized to produce energy and converted to ala and ser

In gut cells – glu converted to ala

Ala & other amino acids – enter the liver
- nitrogen converted to urea, excreted in the urine
- carbons converted to glucose and ketone bodies – oxidized by various tissues for energy
before the carbon skeleton of amino acids are oxidized, the nitrogen atom must be removed.

nitrogen atom from AA - formed ammonia (NH₃) – toxic to the body

in liver NH₃ and –NH₂ group from AA - converted to urea
ROLE of GLUTAMATE in METABOLISM of AMINO ACID NITROGEN

• glu play role in synthesis and degradation of amino acids

Role of glutamate in AA synthesis

• glu obtains N from other amino acid by
  - transamination reaction
  - from NH$_4^+$ by glu dehydrogenase reaction

• transfer NH$_2$ group from glu to $\alpha$-ketoacid $\rightarrow$ produce corresponding amino acid
Role glutamate on AA degradation

_glutamate collect N from other amino acids by transamination reaction_

_glutamate some of this N - released as NH$_3$ by glut dehydrogenase reaction_
Role of glutamate in metabolism of AA nitrogen
Glutamate can collect nitrogen from other amino acids (from transamination reactions) – then release NH$_3$ via glutamate DH reaction.

His - directly deaminated to form NH$_4^+$

Ser and thr - dehydrated, need PLP - form NH$_4^+$

Gln and asn - deamidated - form NH$_4^+$, glu and asp, catalyzed by glutaminase / asparaginase.
UREA CYCLE

STEPS

- **synthesis of carbamoyl phosphate** (in mitochondria) from \( \text{NH}_4^+ \), \( \text{CO}_2 \) and ATP

- **production of arginine**
  - carbamoyl P + ornitihine → citrulline
  - citrulline transported across mitoch. membrane -enter cytosol
  - in cytosol, citrulline + aspartate → arginino-succinate, cleave by argininosuccinase → fumarate + arginine

- Arginine cleave by arginase → urea + ornitihine
  ornithine transported into mitoch, for another round of the cycle
Urea excretion in fasting

- **Fasting** - important role of liver to maintain blood glucose
  - AA from muscle protein → substrate for gluconeogenesis
    - AA → C atom → glucose
    - N atom → urea
  - → urea excretion ↑ in fasting state

- **Prolonged fasting**
  - Brain → did not depend on glucose, use ketone bodies as energy
  - → sparing blood glucose – less muscle protein is cleaved to
    provide AA for gluconeogenesis → urea excretion ↓
Transfer of -NH$_2$ group between AA

- Non essential AA – can be synthesized from its keto acid (if needed), via transfer of -NH$_2$ group from AA to keto acid, catalyzed by transaminase or aminotransferase.

- Transfer of -NH$_2$ also occurs in the degradation of AA.

- Reaction is reversible – in hyperammononemia – disturbance in N excretion – supplementation of keto acid in the diet.

- Example of transaminase – SGOT (=AST), SGPT (=ALT).
Transamination reaction.

- the major process for removing nitrogen from amino acids
- nitrogen transferred from original amino acids to $\alpha$-ketoglutarate $\rightarrow$ glutamate + $\alpha$-ketoacid, catalyzed by transaminase, pyridoxal phosphate (PLP) as cofactor

[Diagram showing the transamination reaction]

- all amino acids (except lys & thr) – can undergo transamination
Oxidative deamination.

- Nitrogen of certain amino acids released as ammonia (NH$_3$) or ammonium (NH$_4^+$).

- Glutamate (glu) oxidatively deaminated by glutamate dehydrogenase (Glu DH), produces NH$_4^+$ + α-ketoglutarate.
  - NAD$^+$ or NADP$^+$ as cofactor.
  - Occur in mitochondria.
Enzymes important in the process of inter conversion of amino acids and removing nitrogen

- transaminase
- glutamate dehydrogenase
- deaminase

Conversion of amino acid nitrogen to urea – occur mainly in the liver – through urea cycle – from precursor

- $\text{NH}_4^+$
- $\text{CO}_2$
- ATP
- nitrogen of aspartate
NITROGEN BALANCE

Healthy adult - N balance N (N intake = N excreted as urea))

In well fed state – N excreted – come from
  • Intake of protein >> or
  • Normal “turnover” protein

Positive N balance  ➔ N intake > N excreted
  • Growth & development
  • Pregnancy
  • Convalescence

Negative N balance  ➔ N excreted > N intake
  • Starvation
  • Disease
  • Deficiency of essential AA
N- containing product from AA

- Cellular protein
- Hormone (tyroxine, epinephrine, insulin)
- Neurotransmitter
- Creatine-P
- Heme of Hb, Mb, cytochrome
- Melanine pigment
- Purine and pirimidine base
N-CONTAINING COMPOUND FROM AMINO ACIDS

1. Creatine

- synthesized from gly, arg and S-adenosylmethionine (SAM)
- + ATP $\rightarrow$ creatine P (stores and transport high energy phosphate within cells)
- creatine P spontaneously $\rightarrow$ creatinine (excreted in urine)
- serum creatinine - indicator of GFR of the kidney
- urinary creatinine - assessing the quantity of other compounds excreted in the urine
2. Glycine

used for conjugation reaction with other compounds (in phase II xenobiotic metabolism) - increased water solubility - easier to excrete in the urine (bile salts, metabolites, drugs)

3. Heme

produced by condensation of gly and succ CoA $\rightarrow$ $\delta$-aminolevulinic acid, precursor of heme
4. Purine base ring

entire gly molecule incorporated into ring + other N provided by gln and asp + CO$_2$ + tetrahydrofolate

5. Pyrimidine base ring - formed from asp + carbamoyl P

6. Neurotransmitter, hormone, pigment

γ-aminobutyric acid (GABA), histamine, serotonin, dopamine, norepinephrine, epinephrine, insulin, thyroid hormone, NO$_2$, melamine
INTEGRATION OF METABOLISM

In well fed state

- After meal – fuels are oxidized – to meet our energy needs

- Any excess of fuel is stored
  - mainly as triacylglycerol in adipose tissue
  - as glycogen in muscle and liver

- Amino acids – converted to body proteins, particularly in muscle
During fasting

1 hour after meal – blood glucose ↓ - insulin ↓, glucagon

Liver glycogenolysis ↑ - supplying glucose to the blood

Adipose tissue lipolysis ↑ - glycerol ↑ and FFA ↑ in blood

FFA – major fuel that oxidized by muscle and liver

Liver use FA to produce ketone bodies – to the blood – taken up by extrahepatic tissues for energy

Brain & erythrocyte – use glucose as energy
As fasting progress

- Liver produce glucose from gluconeogenesis – from substrate glycerol, lactate, glucogenic amino acid
- If C atom of AA converted to glucose – the N atom converted to urea → urea excretion ↑

Prolonged fasting

- Muscle decreases its use of ketone bodies – ketone bodies ↑ in blood
- Brain oxidizes ketone bodies as energy – brain need less glucose – liver decreases its rate of gluconeogenesis – muscle protein is spared – because degradation of protein to AA ↓ → urea excretion ↓
Thank you